

# WEST Search History

DATE: Wednesday, October 15, 2003

## Set Name Query

side by side

## Hit Count Set Name

result set

*DB=USPT; PLUR=YES; OP=AND*

L1	urethral.clm. same secretion\$.clm.	3	L1
L2	male.clm. same secretion\$.clm.	11	L2
L3	urethra.clm. and loop.clm.	54	L3
L4	urethra.clm. and loop.clm. and (acid or pH or sensor or detector)	12	L4
L5	ph near5 sensor\$	2650	L5
L6	L5 same penis	0	L6
L7	L5 same penal	0	L7
L8	L5 same ureth\$	17	L8
L9	L5 same urin\$	19	L9
L10	L5 same seminal\$	0	L10
L11	L5 same sperm\$	1	L11
L12	L5 same loop\$	92	L12
L13	L12 same handle	0	L13
L14	L12 same holder	0	L14
L15	(l8 or l9 or l11) and l12	4	L15
L16	(urethr\$ or penal or penis) near10 loop near10 (sample or fluid or liquid or collect\$)	3	L16
L17	catheter near10 ph	238	L17
L18	L17 same loop\$	2	L18
L19	L17 same (sample or fluid or liquid or collect\$)	101	L19
L20	l19 and (vagin\$ or urethra\$ or penis or penal or cervic\$)	45	L20

L21	l19 same (vagin\$ or urethra\$ or penis or penal or cervic\$)	1	L21
L22	sampl\$ naer10 loop	0	L22
L23	sampl\$ near10 loop	10293	L23
L24	L23 same urine	27	L24
L25	ph near \$sensor	1346	L25
L26	L25 same handle	4	L26
L27	loop.ti,ab.	48033	L27
L28	L27 and handle.clm.	1954	L28
L29	L28 and (vagina\$ or cervic\$)	26	L29
L30	ph near5 handle	81	L30

END OF SEARCH HISTORY

# WEST Search History

DATE: Wednesday, October 15, 2003

## Set Name Query

side by side

## Hit Count Set Name

result set

*DB=USPT; PLUR=YES; OP=AND*

L1	(method or process).clm. and (metronidazole or itraconazole or ofloxacin).clm.	312	L1
L2	L1 and protoz\$.clm.	17	L2
L3	L1 and protoz\$.clm. and itraconazole.clm.	2	L3

END OF SEARCH HISTORY

copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

64. The method of claim 59, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

65. The method of claim 59, wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

66. The method of claim 65, wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

67. A method of treating an infection in a human or animal caused by a virus comprising the step of:

administering an effective amount of a composition nonionic block copolymer into the human or animal, wherein the copolymer has the following general formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and approximately 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and approximately 50% of the copolymer.

68. The method of claim 67 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

69. The method of claim 67, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

70. The method of claim 67, wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

71. The method of claim 67, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

72. The method of claim 67, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

73. The method of claim 67, wherein the composition further comprises approximately 0.1% to approximately

5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of a low molecular weight alcohol.

74. The method of claim 73, wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

75. A method of treating a human or animal comprising administering to a human or animal infected with a virus a therapeutic drug and a nonionic block copolymer, wherein the block copolymer has the following formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and 50% of the copolymer.

76. The method of claim 75, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

77. The method of claim 75, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

78. The method of claim 75, wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

79. The method of claim 75, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

80. The method of claim 75, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

81. The method of claim 76, wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of a low molecular weight alcohol.

82. The method of claim 81, wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

83. The method of claim 1 wherein the bacteria is selected from the group consisting of *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium leprae*, *Chlamydia trachomatis*, *Chlamydia pneumoniae*, *Chlamydia psittaci* and *Listeria monocytogenes*.

84. The method of 67, wherein the virus is HIV or herpes or antigenically-related strains thereof.
85. The method of claim 59, wherein the protozoa is a Toxoplasma species.
86. The method of claim 75, wherein the virus is HIV or herpes or antigenically-related strains thereof.

WEST



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L2: Entry 16 of 17

File: USPT

Apr 8, 1997

DOCUMENT-IDENTIFIER: US 5618564 A

TITLE: Composition for the treatment of helicobacter pylori infection

## CLAIMS:

1. A method for the therapy of a Helicobacter pylori infected patient, which comprises blocking a part of the patient's superior duodenal angulus to prevent gastric contents from leaking into the small intestine, then directly instilling a composition which contains, as active ingredients, a protease and an antibacterial agent into the patient's stomach thereby treating the gastric wall through exposure of said wall to said composition for a predetermined period of time in which the position of the patient is changed, and recovering the gastric contents from the patient's stomach after the treatment.
2. The method of claim 1, wherein the protease is selected from the group consisting of pronase, trypsin, .alpha.-chymotrypsin, serrapeptase, bromelain and pepsin.
3. The method of claim 2, wherein the protease is pronase.
4. The method of claim 3, wherein the amount of pronase is 0.02 to 0.1% by weight.
5. The method of claim 1, wherein the amount of antibacterial agent is 3 to 10% by weight in a total.
6. The method of claim 1, wherein the antibacterial agent is selected from the group consisting of an antibiotic, an anti-protozoan drug and a bismuth preparation.
7. The method of claim 6, wherein the antibiotic is selected from the group consisting of amoxicillin, erythromycin and clindamycin.
8. The method of claim 6, wherein the anti-protozoan drug is selected from the group consisting of metronidazole and tinidazole.
9. The method of claim 6, wherein the bismuth preparation is selected from the group consisting of bismuth, bismuth subnitrate, bismuth subsalicylate and colloidal bismuth.
10. The method of claim 6, wherein the composition comprises as the antibacterial agents amoxicillin, metronidazole and bismuth subnitrate.
11. The method of claim 10, wherein the amount of bismuth subnitrate is 1 to 4% by weight, the amount of

amoxicillin is 1 to 4% by weight and the amount of metronidazole is 1 to 2% by weight.

12. The method of claim 1, wherein the composition is a solution.



**WEST****End of Result Set**

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L2: Entry 17 of 17

File: USPT

Oct 23, 1984

DOCUMENT-IDENTIFIER: US 4478822 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Drug delivery system utilizing thermosetting gels

## CLAIMS:

1. An aqueous pharmaceutical composition for rectal, urethral, nasal, vaginal, optical or oral in the buccal pouch administration to a body cavity to treat a condition requiring pharmacological treatment comprising
  - a. 10% to 50% by weight of a polymer of the formula: **##STR2##** wherein w is an integer of from 2-6 containing approximately 40% to 80% poly(oxyethylene) and approximately 20 to 60% poly(oxypropylene) and having a molecular weight of 7,000 to 50,000; and x and y are any integers within the above constraints; and
  - b. a pharmacologically effective amount of drug selected from the group consisting of anti-bacterial substances, antihistamines and decongestants, anti-inflammatories, anti-parasitics, antiviral, local anesthetics, antifungal, amebecidal, or trichomonocidal agents, analgesics, antiarthritics, antiasthmatics, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, and muscle relaxants and anti-protozoals; and
  - c. a pharmaceutically acceptable acid or base being in sufficient quantity to adjust the pH of the composition to range from 2 to 9 and wherein the composition is liquid at about room temperature or below.
11. The composition of claim 1 wherein the antifungal, antiprotozoal, amebecidal or trichomonocidal agent is selected from the group consisting of polyoxyethylene nonylphenol, alkylaryl sulfonate, oxyquinoline sulfate, miconazole nitrate, sulfanilamide, condicidin, sulfoxazole, nystatin, clotrimazole, metronidazole, chloramphenicol, chloroquine, trimethoprim or sulfamethoxazole.
28. A method of treating a condition requiring pharmacological treatment which comprises administering rectal, urethral, nasal, vaginal, optical or oral in the buccal pouch to a body cavity a liquid drug delivery device comprising:
  - a. 10% to 50% by weight of a polymer of the formula **##STR3##** wherein w is an integer of from 2 to 6 containing approximately 40% to 80% poly(oxyethylene) and approximately 20-60% poly(oxypropylene) and having a molecular weight of 7,000 to 50,000; and x and y are any integers within the above constraints; and
  - b. a pharmacologically effective amount of drug selected from the group consisting of antibacterial

substances, antihistamines and decongestants, anti-inflammatories, antiparasitics, antivirals, local anesthetics, antifungal, amebecidal, or trichomonocidal agents, analgesics, antiarthritics, antiasthmatics, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, muscle relaxants and antiprotozoals; and

c. a pharmaceutically acceptable acid or base being in sufficient quantity to adjust the pH of the composition to range from 2 to 9 and wherein the composition is liquid at about room temperature or below.

29. A method of treatment according to claim 28 wherein the polymer is one wherein w is 2.

30. A method of treatment according to claim 23 wherein the polymer is Tetronic.RTM.1307.

31. A method of treatment according to claim 28 wherein the gel-sol transition temperature of the composition is room temperature or below and said composition is liquid at this temperature.

32. A method of treatment of claim 28 wherein said pharmaceutical composition is administered rectally, urethrally, nasally, vaginally, otically or orally within the buccal pouch.

33. A method of treatment according to claim 28 wherein the antibacterial substances are selected from the group consisting of beta-lactam antibiotics, tetracyclines, chloroamphenicol, neomycin, gramicidin, bacitracin, sulfonamides, aminoglycoside antibiotics, tobramycin, nitrofurazone, nalidixic acid and analogs and the antimicrobial combination of fludalanine/pentizidone.

34. A method of treatment according to claim 28 wherein the antihistaminics and decongestants are selected from the group consisting of perilamine, chlorpheniramine, tetrahydrozoline and antazoline.

35. A method of treatment according to claim 28 wherein the anti-inflammatory drugs are selected from the group consisting of cortisone, hydrocortisone, betamethasone, dexamethasone, fluocortolone, prednisolone, triamcinalone, sulindac and its salts and corresponding sulfide.

36. A method of treatment of claim 28 wherein the antiparasitic compound is ivermectin.

37. A method of treatment according to claim 28 wherein the antiviral effective compounds are selected from the group consisting of acyclovir and interferon.

38. A method of treatment according to claim 28 wherein the local anesthetics are selected from the group consisting of benzocaine, lidocaine and procaine.

39. A method of treatment according to claim 28 wherein the antifungal, antiprotozoal, amebecidal or trichomonocidal agent is selected from the group consisting of polyoxyethylene nonylphenol, alkylaryl sulfonate, oxyquinoline sulfate, miconazole nitrate, sulfonilamide, condicidin, sulfisoxazole, nystatin, clotrimazole metronidazole, chloramphenicol, chloroquine, trimethoprim or sulfamethoxazole.

40. A method of treatment according to claim 28 wherein the analgesic drug is selected from the group consisting of diflunisal, aspirin or acetaminophen.

41. A method of treatment according to claim 28 wherein the antiarthritics are selected from the group consisting of phenylbutazone, indomethacin, sulindac and its salts and corresponding sulfide, dexamethasone, ibuprofen, allopurinol, oxyphenbutazone or probenecid.

42. A method of treatment according to claim 28 wherein the antiasthma drugs are selected from the group consisting of theophylline, ephedrine, beclomethasone dipropionate and epinephrine.
43. A method of treatment according to claim 28 wherein the anticoagulants are selected from the group consisting of heparin, bishydroxycoumarin, and warfarin.
44. A method of treatment according to claim 28 wherein the anticonvulsants are selected from the group consisting of diphenylhydantoin and diazepam.
45. A method of treatment according to claim 28 wherein the antidepressants are selected from the group consisting of amitriptyline, chlordiazepoxide perphenazine, protriptyline, imipramine and doxepin.
46. A method of treatment according to claim 28 wherein the antidiabetics are selected from the group consisting of insulin, tolbutamide, tolazamide, acetohexamide and chlorpropamide.
47. A method of treatment according to claim 28 wherein the antineoplastics are selected from the group consisting of adriamycin, flurouracil, methotrexate and asparaginase.
48. A method of treatment according to claim 28 wherein the antipsychotics are selected from the group consisting of prochlorperazine lithium carbonate, lithium citrate, thioridazine, molindone, fluphenazine, trifluoperazine, perphenazine, amitriptyline and triflupromazine.
49. A method of treatment according to claim 28 wherein the antihypertensives are selected from the group consisting of spironolactone, methyldopa, hydralazine, clonidine, chlorothiazide, deserpidine, timolol, propranolol, metoprolol, prazosin hydrochloride and reserpine.
50. A method of treatment according to claim 28 wherein the muscle relaxants are selected from the group consisting of mephalan, danbrolene, cyclobenzaprine, methocarbamol and diazepam.
51. A method of treatment according to claim 28 wherein the composition includes a buffering agent or salt of from 0% to 5% by weight of the composition.
52. A method of treatment according to claim 51 wherein the buffering agent or salt is selected from the group consisting of alkali or alkali earth carbonates, chlorides, sulfates, phosphates, bicarbonates, citrates, borates, acetates and succinates.
53. A method of treatment according to claim 28 wherein the composition includes from 0.001% to 5% by weight of the composition of a preservative.
54. A method of treatment according to claim 53 wherein the preservatives are selected from the group consisting of sodium bisulfite, sodium thiosulfate, ascorbate, benzalkonium chloride, chlorobutanol, thimerosal, phenylmercuric borate, parabens, benzylalcohol and phenylethanol.
55. A method of treatment according to claim 28 wherein the acid or base is selected from the group consisting of hydrochloric acid or sodium hydroxide.

**WEST****End of Result Set**

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L3: Entry 2 of 2

File: USPT

Sep 25, 2001

DOCUMENT-IDENTIFIER: US 6294192 B1

TITLE: Triglyceride-free compositions and methods for improved delivery of hydrophobic therapeutic agents

**CLAIMS:**

38. The capsule of claim 36, wherein the therapeutic agent is selected from the group consisting of analgesics, anti-inflanunatory agents, anthelmintics, anti-arrhythmic agents, anti-bacterial agents, anti-viral agents, anti-coagulants, anti-depressants, anti-diabetics, anti-epileptics, anti-fungal agents, anti-gout agents, anti-hypertensive agents, anti-malarials, anti-migraine agents, anti-muscarinic agents, anti-neoplastic agents, erectile dysfunction improvement agents, immunosuppressants, anti-protozoal agents, anti-thyroid agents, anxiolytic agents, sedatives, hypnotics, neuroleptics, .beta.-blockers, cardiac inotropic agents, corticosteroids, diuretics, anti-parkinsonian agents, gastro-intestinal agents, histamine H.sub.1 and H.sub.2 receptor antagonists, keratolytics, lipid regulating agents, anti-anginal agents, nutritional agents, opioid analgesics, sex hormones, stimulants, muscle relaxants, anti-osteoporosis agents, anti-obesity agents, cognition enhancers, anti-urinary incontinence agents, nutritional oils, anti-benign prostate hypertrophy agents, essential fatty acids, non-essential fatty acids, and mixtures thereof.

39. The capsule of claim 36, wherein the therapeutic agent is tramadol, celecoxib, etodolac, refocoxib, oxaprozin, leflunomide, diclofenac, nabumetone, ibuprofen, flurbiprofen, tetrahydrocannabinol, capsaicin, ketorolac, albendazole, ivermectin, amiodarone, zileuton, zafirlukast, albuterol, montelukast, azithromycin, ciprofloxacin, clarithromycin, dirithromycin, rifabutine, rifapentine, trovafloxacin, baclofen, ritanovir, saquinavir, nelfinavir, efavirenz, dicournarol, tirofibrin, cilostazol, ticlidopine, clopidrogel, oprevelkin, paroxetine, sertraline, venlafaxine, bupropion, clomipramine, miglitol, repaglinide, glymepride, pioglitazone, rosigiltazone, troglitazone, glyburide, glipizide, glibenclamide, carbamezepine, fosphenytion, tiagabine, topiramate, lamotrigine, vigabatrin, amphotericin B, butenafine, terbinafine, itraconazole, flucanazole, miconazole, ketoconazole, metronidazole, griseofulvin, nitrofurantoin, spironolactone, lisinopril, benezepril, nifedipine, nilsolidipine, telmisartan, irbesartan, eposartan, valsartan, candesartan, minnoxidil, terazosin, halofantrine, mefloquine, dihydroergotamine, ergotamine, frovatriptan, pizofetin, sumatriptan, zolmitriptan, naratriptan, rizatriptan, aminogluthemide, busulphan, cyclosporine, mitoxantrone, irinotecan, etoposide, teniposide, paclitaxel, tacrolimus, sirolimus, tamoxifen, camptothecan, topotecan, nilutamide, bicalutamide, pseudo-ephedrine, toremifene, atovaquone, metronidazole, furazolidone, paricalcitol, benzonatate, mnidazolam, zolpidem, gabapentin, zopiclone, digoxin, beclomethsone, budesonide, betamethasone, prednisolone, cisapride, cimetidine, loperamide, famotidine, lansoprazole, rabeprazole, nizatidine, omeprazole, citrizine, cinnarizine, dexchlorpheniramine, loratadine, clemastine, fexofenadine, chlorpheniramine, acutretin, tazarotene, calciprotiene, calcitriol, targretin, ergocalciferol, cholecalciferol, isotretinoin, tretinoin, calcifediol, fenofibrate, probucol, gemfibrozil, cerivistatin, pravastatin, simvastatin, fluvastatin, atorvastatin, tizanidine,

dantrolene, isosorbide dinatrate, a carotene, dihydrotachysterol, vitamin A, vitamin D, vitamin E, vitamin K, an essential fatty acid source, codeine, fentanyl, methadone, nalbuphine, pentazocine, clomiphene, danazol, dihydro epiandrosterone, medroxyprogesterone, progesterone, rimexolone, megesterol acetate, osteradiol, finasteride, mifepristone, amphetamine, L-thyroxine, tamsulosin, methoxsalen, tacrine, donepezil, raloxifene, vertoporphin, sibutramine, pyridostigmine, a pharmaceutically acceptable salt, isomer, or derivative thereof, or a mixture thereof.

40. The capsule of claim 1, wherein the hydrophobic therapeutic agent is selected from the group consisting of tramadol, celecoxib, etodolac, refocoxib, oxaprozin, leflunomide, diclofenac, nabumetone, ibuprofen, flurbiprofen, tetrahydrocannabinol, capsaicin, ketorolac, albendazole, ivermectin, amiodarone, zileuton, zafirlukast, albuterol, montelukast, azithromycin, ciprofloxacin, clarithromycin, dirithromycin, rifabutine, rifapentine, trovafloxacin, baclofen, ritanovir, saquinavir, nelfinavir, efavirenz, miglitol, repaglinide, glymepride, pioglitazone, rosiglitazone, troglitazone, glyburide, glipizide, glibenclamide, carbamazepine, fosphenytoin, tiagabine, topiramate, lamotrigine, vigabatrin, amphotericin B, butenafine, terbinafine, itraconazole, fluconazole, miconazole, ketoconazole, metronidazole, griseofulvin, nitrofurantoin, spironolactone, halofantrine, mefloquine, dihydroergotamine, ergotamine, frovatriptan, pizofetin, sumatriptan, zolmitriptan, naratriptan, rizatriptan, aminoglutethimide, busulphan, cyclosporine, mitoxantrone, irinotecan, etoposide, teniposide, paclitaxel, tacrolimus, sirolimus, tamoxifen, camptothecin, topotecan, nilutamide, bicalutamide, pseudo-ephedrine, toremifene, atovaquone, metronidazole, furzolidone, paricalcitol, benzonatate, midazolam, zolpidem, gabapentin, zopiclone, digoxin, cisapride, cimetidine, loperamide, famotidine, lansoprazole, rabeprazole, nizatidine, omeprazole, citrizine, cinnarizine, dexchlorpheniramine, loratadine, clemastine, fexofenadine, chlorpheniramine, acutretin, tazarotene, calcipotriene, calcitriol, targretin, ergocalciferol, cholecalciferol, isotretinoin, tretinoin, calcifediol, fenofibrate, probucol, gemfibrozil, cerivastatin, pravastatin, simvastatin, fluvastatin, atorvastatin, tizanidine, dantrolene, carotenes, dihydrotachysterol, vitamin A, vitamin D, vitamin E, vitamin K, essential fatty acid sources, codeine, fentanyl, methadone, nalbuphine, pentazocine, clomiphene, danazol, dihydro epiandrosterone, medroxyprogesterone, progesterone, rimexolone, megesterol acetate, osteradiol, finasteride, mifepristone, amphetamine, L-thyroxine, tamsulosin, methoxsalen, tacrine, donepezil, raloxifene, vertoporphin, sibutramine, pyridostigmine, pharmaceutically acceptable salts, isomers and derivatives thereof, and mixtures thereof.

41. The capsule of claim 1, wherein the therapeutic agent is selected from the group consisting of tramadol, celecoxib, etodolac, refocoxib, oxaprozin, leflunomide, diclofenac, nabumetone, ibuprofen, flurbiprofen, tetrahydrocannabinol, capsaicin, ketorolac, ivermectin, amiodarone, zileuton, zafirlukast, albuterol, montelukast, rifabutine, rifapentine, trovafloxacin, baclofen, ritanovir, saquinavir, nelfinavir, efavirenz, miglitol, repaglinide, glymepride, pioglitazone, rosiglitazone, troglitazone, glyburide, glipizide, glibenclamide, carbamazepine, fosphenytoin, tiagabine, topiramate, lamotrigine, vigabatrin, terbinafine, itraconazole, fluconazole, miconazole, ketoconazole, metronidazole, nitrofurantoin, dihydroergotamine, ergotamine, frovatriptan, pizofetin, zolmitriptan, pseudo-ephedrine, naratriptan, rizatriptan, aminoglutethimide, busulphan, cyclosporine, mitoxantrone, irinotecan, etoposide, teniposide, paclitaxel, tacrolimus, sirolimus, tamoxifen, camptothecin, topotecan, nilutamide, bicalutamide, toremifene, atovaquone, metronidazole, furzolidone, paricalcitol, benzonatate, cisapride, cimetidine, loperamide, famotidine, lansoprazole, rabeprazole, nizatidine, omeprazole, citrizine, cinnarizine, dexchlorpheniramine, loratadine, clemastine, fexofenadine, chlorpheniramine, acutretin, tazarotene, calcipotriene, calcitriol, targretin, ergocalciferol, cholecalciferol, isotretinoin, tretinoin, calcifediol, fenofibrate, probucol, simvastatin, atorvastatin, tizanidine, dantrolene, carotenes, dihydrotachysterol, vitamin A, vitamin D, vitamin E, vitamin K, essential fatty acid sources, danazol, dihydro epiandrosterone, medroxyprogesterone, progesterone, rimexolone, megesterol acetate, osteradiol, finasteride, mifepristone, raloxifene, L-thyroxine, tamsulosin, methoxsalen, pharmaceutically acceptable salts, isomers and derivative thereof, and mixtures thereof.

42. The capsule of claim 1, wherein the hydrophobic therapeutic agent is selected from the group consisting of

sildenafil citrate, amlodipine, tramadol, celecoxib, refocoxib, oxaprozin, nabumetone, ibuprofen, terbenafine, itraconazole, zileuton, zafirlukast, cisapride, fenofibrate, tizanidine, nizatidine, fexofenadine, loratadine, famotidine, paricalcitol, atovaquone, nabumetone, tetrahydrocannabinol, megestrol acetate, repaglinide, progesterone, rimexolone, cyclosporine, tacrolimus, sirolimus, teniposide, paclitaxel, pseudo-ephedrine, troglitazone, rosiglitazone, finasteride, vitamin A, vitamin D, vitamin E, pharmaceutically acceptable salts, isomers and derivatives thereof, and mixtures thereof.

62. A method of treating an animal with a hydrophobic therapeutic agent, the method comprising:

orally administering to the animal a dosage form comprising the capsule of claim 1.

63. The method of claim 62, wherein the animal is a mammal.

64. The method of claim 63, wherein the mammal is a human.

# WEST Search History

DATE: Wednesday, October 15, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit</u> <u>Count</u>	<u>Set</u> <u>Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=AND</i>			
L1	periodic.clm.	34566	L1
L2	L1 and colon\$.clm.	23	L2
L3	period\$ near5 colon\$	1316	L3
L4	L3 and protoz\$	71	L4
L5	L4 and refract\$	13	L5
L6	period\$ near3 grow\$	13206	L6
L7	L6 same protoz\$	14	L7
L8	L6 same colon\$	409	L8
L9	L6 near5 colon\$	93	L9
L10	periodic\$ near3 grow\$	1242	L10
L11	L10 near5 colon\$	4	L11
L12	L11 same protozo\$	0	L12
L13	L11 same refract\$	0	L13
L14	periodic\$ near3 cluster\$	220	L14
L15	L14 and protoz\$	3	L15
L16	periodic\$ near3 colon\$ near5 cluster\$	0	L16

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L2: Entry 2 of 17

File: USPT

Aug 27, 2002

DOCUMENT-IDENTIFIER: US 6440936 B2

TITLE: Anti-protozoan methods and materials

## CLAIMS:

1. A method of treating a protozoan infection comprising administering to a subject infected with a protozoan species selected from the group consisting of *Toxoplasma gondii*, *Leishmania* species, *Trypanosoma cruzi*, and *Plasmodium* species: a) an anti-protozoan agent selected from the group consisting of chloroquine, quinine, mefloquine, amodiaquine, primaquine, pyrimethamine, sulfadoxine, sulfadiazine, trimethoprim, pentavalent antimony, pentamidine, amphotericin B, rifampin, metronidazole, ketoconazole, benznidazole and nifurtimox, and b) a bactericidal/permeability-increasing (BPI) protein product, said BPI protein product being BPI holoprotein, a BPI fragment, a BPI variant, a BPI analog, or a BPI-derived peptide, or dimeric forms thereof,

wherein said anti-protozoan agent and BPI protein product are administered in therapeutically effective amounts.

2. The method of claim 1 wherein the protozoan species is *Toxoplasma gondii*.

3. The method of claim 1 wherein the protozoan species is a *Leishmania* species.

4. The method of claim 1 wherein the protozoan species is *Trypanosoma cruzi*.

5. The method of claim 1 wherein the *Plasmodium* species is *Plasmodium vivax*.

6. The method of claim 1 wherein the *Plasmodium* species is *Plasmodium falciparum*.

7. The method of claim 1 wherein the *Plasmodium* species is *Plasmodium ovale*.

8. The method of claim 1 wherein the *Plasmodium* species is *Plasmodium malariae*.

9. A method of killing or inhibiting growth of a protozoa comprising contacting a protozoa from a species selected from the group consisting of *Toxoplasma gondii*, *Leishmania* species, *Trypanosoma cruzi*, and *Plasmodium* species with: a) an anti-protozoan agent selected from the group consisting of chloroquine, quinine, mefloquine, amodiaquine, primaquine, pyrimethamine, sulfadoxine, sulfadiazine, trimethoprim, pentavalent antimony, pentamidine, amphotericin B, rifampin, metronidazole, ketoconazole, benznidazole and nifurtimox, and b) a bactericidal/permeability-increasing (BPI) protein product, said BPI protein product being BPI holoprotein, a BPI fragment, a BPI variant, a BPI analog, or a BPI-derived peptide, or dimeric forms thereof,



wherein said anti-protozoan agent and BPI protein product are administered in amounts effective to kill or inhibit growth of said protozoa.

10. The method of claim 9 wherein the protozoan species is *Toxoplasma gondii*.
11. The method of claim 9 wherein the protozoan species is a *Leishmania* species.
12. The method of claim 9 wherein the protozoan species is *Trypanosoma cruzi*.
13. The method of claim 9 wherein the *Plasmodium* species is *Plasmodium vivax*.
14. The method of claim 9 wherein the *Plasmodium* species is *Plasmodium falciparum*.
15. The method of claim 9 wherein the *Plasmodium* species is *Plasmodium ovale*.
16. The method of claim 9 wherein the *Plasmodium* species is *Plasmodium malariae*.

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L2: Entry 5 of 17

File: USPT

Aug 28, 2001

DOCUMENT-IDENTIFIER: US 6280768 B1

TITLE: Berberine alkaloids as a treatment for chronic protozoally induced diarrhea

## CLAIMS:

1. A method for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea in a patient comprising administering to the patient an effective amount of a berberine alkaloid, and continuing the administration for a sufficient time to substantially alleviate the chronic diarrhea is induced by protozoa selected from the group consisting of Microsporidia spp. and Cryptosporidia spp.
2. The method of claim 1 wherein the berberine alkaloid is selected from the group consisting of berberine hydrochloride, berberine, berberrubine, coreximine, tetrahydropalmatine, jatrorrhizine, 13-hydroxyberberine chloride, coralyne chloride, 7,8-dihydro-13-methylberberine, berberine acetone, 13-allylberberine, palmatine, and 13-benzylberberine.
3. The method of claim 1 wherein the berberine alkaloid is berberine hydrochloride.
4. The method of claim 1 wherein the administration is enteral.
5. The method of claim 1 wherein the alleviation of symptoms of chronic diarrhea is characterized by the absence of Microsporidia.
6. The method of claim 1 wherein the patient is a human patient.
7. The method of claim 1 wherein the patient is immunosuppressed.
8. The method of claim 6 wherein the patient is infected with human immunodeficiency virus.
9. The method of claim 1 wherein the patient is a veterinary patient.
10. A composition for the treatment or alleviation of symptoms of chronic diarrhea induced by protozoa selected from the group consisting of Blastocystis hominis, Dientamoeba fragilis, Balantidium coli, Isopora belli, and Cyclospora cayetanensis, comprising a berberine alkaloid and a pharmaceutically acceptable carrier.
11. The method of claim 1 wherein an antiprotozoal agent is administered prior to, subsequent to, or concurrently with the berberine alkaloid.

12. The method of claim 11 wherein the antiprotozoal agent is albendazole or metronidazole.
13. A composition for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea in a patient comprising a berberine alkaloid selected from the group consisting of berberine and berberine hydrochloride, an antiprotozoal agent selected from the group consisting of albendazole and metronidazole, and a pharmaceutically acceptable carrier, wherein said diarrhea is induced by protozoa selected from the group consisting of Microsporidia spp. and Cryptosporidia spp.
14. A composition for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea in a patient comprising a berberine alkaloid selected from the group consisting of berberrubine, coreximine, tetrahydropalmatine, jatrorrhizine, 13-hydroxyberberine chloride, coralyne chloride, 7,8-dihydro-13-methylberberine, berberine acetone, 13-allylberberine, palmatine, and 13-benzylberberine; an antiprotozoal agent selected from the group consisting of albendazole and metronidazole; and a pharmaceutically acceptable carrier, wherein said diarrhea is induced by protozoa selected from the group consisting of Microsporidia spp. and Cryptosporidia spp.
15. The composition of claim 13 wherein the antiprotozoal agent is metronidazole.
16. The composition of claim 14 wherein the antiprotozoal agent is metronidazole.
17. The method of claim 1 in which the protozoa are Enterocytozoon bienersi, Encephalitozoon intestinalis or Cryptosporidium parvum.
18. The method of claim 8 in which the protozoa are Enterocytozoon bienersi, Encephalitozoon intestinalis or Cryptosporidium parvum.
19. The method of claim 12 in which the antiprotozoal agent is albendazole.
22. A method for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea in a patient comprising administering to the patient an effective amount of a berberine alkaloid, and continuing the administration for a sufficient time to substantially alleviate the chronic diarrhea is induced by protozoa selected from the group consisting of Blastocystis hominis, Dientamoeba fragilis Balantidium coli, Isoipora belli, and Cyclospora cayentanensis.
24. The composition of claim 13 or 14 in which the protozoa are Microspordia spp.
26. The composition of claim 13 or 14 in which the protozoa are Cryptosporidia spp.
28. The method of claim 1 in which berberine alkaloid is administered at a dosage of about 300 to about 1500 mg per day.
29. The method of claim 28 in which the dosage is about 450 to about 900 mg per day.
30. The method of claim 1 in which the patient is non-immunosuppressed.
31. A composition for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea induced by Microsporidia spp. or Cryptosporidia spp. in a patient comprising a berberine alkaloid selected from the group consisting of berberine and berberine hydrochloride and a pharmaceutically acceptable carrier.
32. A composition for the treatment or alleviation of symptoms of protozoally induced chronic diarrhea

induced by *Microsporidia* spp. or *Cryptosporidia* spp. in a patient, comprising a berberine alkaloid selected from the group consisting of berberrubine, coreximine, tetrahydropalmatine, jatrorrhizine, 13-hydroxyberberine chloride, coralyne chloride, 7,8-dihydro- 13-methylberberine, berberine acetone, 13-allylberberine, palmatine, and 13-benzylberberine.

34. The composition of claim 31 or 32 in which the protozoa are *Enterocytozoon bienersi*, *Encephalitozoon intestinalis* or *Cryptosporidium parvum*.

35. The composition of claim 31 or 32 in which the protozoa are *Microsporidia* spp.

37. The composition of claim 31 or 32 in which the protozoa are *Cryptosporidia* spp.

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L2: Entry 8 of 17

File: USPT

Jun 12, 2001

DOCUMENT-IDENTIFIER: US 6245811 B1

TITLE: Fatty acid esters as bioactive compounds

## CLAIMS:

8. A method of manufacturing a medicament for improving the transport of a drug or other active across lipid membranes in the body or securing an action as set out in claim 7, characterised by use of the active in the form of a compound as in any preceding claim.

9. A method of improving the transport of a drug or other active across lipid membranes in the body, characterised by use of the active in the form of a compound as set out in claim 1.

16. The compound according to claim 10, wherein R.sub.2 is the residue of an antifungal drug selected from the group consisting of metronidazole, antifungal imidazoles and nitroimidazoles, and amphotericin.

28. A method for treating a disorder selected from the group consisting of complications of diabetes; cancer; osteoarthritis; rheumatoid arthritis; inflammatory and auto-immune diseases other than arthritis; respiratory diseases; neurological disorders; renal and urinary tract disorders; cardiovascular disorders; degenerative diseases of the eye; psychiatric disorders; prostatic hypertrophy and prostatitis; impotence and male infertility; mastalgia; male pattern baldness; osteoporosis; dermatological disorders; dyslexia and other learning disabilities; and cancer cachexia; comprising administering to a patient in need thereof an effective amount of the compound of claim 10.

29. The method according to claim 28, wherein said disorder is a complication of diabetes selected from the group consisting of neuropathy, retinopathy, and insufficient response to insulin.

30. The method according to claim 28, wherein said disorder is an inflammatory and autoimmune disease other than arthritis selected from the group consisting of Sjogren's syndrome, systemic lupus, ulcerative colitis, Crohn's disease, and uveitis.

31. The method according to claim 28, wherein said disorder is asthma.

32. The method according to claim 28, wherein said disorder is a neurological disorder selected from the group consisting of multiple sclerosis, Parkinson's disease, and Huntington's chorea.

33. The method according to claim 28, wherein said disorder is a degenerative disease of the eye selected from the group consisting of retinitis pigmentosa and senile macular degeneration.

34. The method according to claim 28, wherein said disorder is a psychiatric disorder selected from the group consisting of schizophrenia, Alzheimer's disease, attention deficit disorder, alcoholism, and depression.

35. The method according to claim 28, wherein said disorder is a dermatological disorder selected from the group consisting of atopic eczema, hand eczema, psoriasis, urticaria, and allergic disorders.

36. The method according to claim 28, wherein said disorder is selected from the group consisting of complications of diabetes; neurological disorders; cardiovascular disorders; degenerative diseases of the eye; psychiatric disorders; dermatological disorders; and dyslexia and other learning disabilities; and wherein R.sup.1 is arachidonic acid (AA) and R.sup.2 is selected from the group consisting of .lambda.-linolenic acid (GLA), dihomom.-lambda.-linolenic acid (DGLA), arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA).

37. The method according to claim 28, wherein said disorder is selected from the group consisting of cancer; osteoarthritis; rheumatoid arthritis; inflammatory and auto-immune diseases other than arthritis; respiratory diseases; neurological disorders; renal and urinary tract disorders; cardiovascular disorders; degenerative diseases of the eye; psychiatric disorders; osteoporosis; dermatological disorders; dyslexia and other learning disabilities; and cancer cachexia; and wherein R.sup.1 is eicosapentaenoic acid (EPA) and R.sub.2 is selected from the group consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

38. The method according to claim 28, wherein said administering comprises oral, topical, enteral or parenteral administration.

39. A method of treating or preventing a nutritional deficiency, comprising administering to a patient in need thereof an effective amount of a compound according to claim 10.

40. The method according to claim 39, wherein administering comprises oral administration of a composition comprising said compound and a food, nutritional supplement, or food additive.

41. The method according to claim 39, said administering comprises enteral or parenteral administration.

43. A method for treating skin disorders comprising applying to the skin or hair of a patient in need thereof the composition of claim 39.

44. A method for treating psychiatric, neurological, behavioral, steep, or pain disorders comprising administering to a patient in need thereof an effective amount of the compound of claim 11, wherein said amino acid is tryptophan.

45. The method according to claim 44, wherein said disorders comprise depression or migraine.

46. A method for treating depression, multiple sclerosis, or chronic fatigue syndrome comprising administering to a patient in need thereof an effective amount of the compound of claim 11, wherein said amino acid is phenylalanine.

47. A method for treating diseases associated with defective nitric oxide production, comprising administering to a patient in need thereof an effective amount of the compound of claim 11, wherein said amino acid is arginine.

48. A method for treating muscle weakness, cardiac failure, chronic fatigue syndrome, Alzheimer's disease, or

peripheral neuropathies, comprising administering to a patient in need thereof an effective amount of the compound of claim 11, wherein said amino acid is carnitine or a carnitine derivative.

49. A method for treating cancer comprising administering to a patient in need thereof an effective amount of the compound of claim 11, wherein said amino acid is aminolevulinic acid.

50. A method for treating muscular dystrophy, cardiac failure, chronic fatigue syndrome, or Alzheimer's disease, comprising administering to a patient in need thereof an effective amount of the compound of claim 12.

51. A method for treating inflammatory disorders of pain, Alzheimer's disease, or for inhibiting platelet aggregation, comprising administering to a patient in need thereof an effective amount of the compound of claim 13.

52. A method of treating or preventing a bacterial infection, comprising administering to a patient in need thereof an effective amount of the compound of claim 14.

53. The method according to claim 52, wherein said bacterial infection comprises acne.

54. The method of treating malaria, protozoal disorders, inflammatory disorders, or schizophrenia, comprising administering to a patient in need thereof an effective amount of the compound of claim 15.

55. A method for treating fungal infections, comprising administering to a patient in need thereof an effective amount of the compound of claim 16.

56. A method for treating skin disorders or asthma, comprising administering to a patient in need thereof an effective amount of the compound of claim 17.

57. A method for treating ovarian deficiency, osteoporosis or testicular deficiency, comprising administering to a patient in need thereof an effective amount of the compound of claim 18.

58. A method of treating disorders associated with aging comprising administering to a patient in need thereof an effective amount of the compound of claim 19.

59. A method for treating dermatological disorders, comprising administering to a patient in need thereof an effective amount of the compound of claim 21.

60. A method for treating autoimmune and inflammatory disorders comprising administering to a patient in need thereof an effective amount of the compound of claim 22.

61. The method according to claim 60, wherein said autoimmune or inflammatory disorders are selected from the group consisting of psoriasis, eczema, asthma, rheumatoid arthritis, and inflammatory bowel disease.

62. A method for treating epilepsy, comprising administering to a patient in need thereof an effective amount of the compound of claim 23.

63. A method of lowering cholesterol level, comprising administering to a patient in need thereof an effective amount of the compound of claim 24.

64. A method for treating cancer cachexia, comprising administering to a patient in need thereof an effective

amount of the compound of claim 10.



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L2: Entry 9 of 17

File: USPT

Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180136 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Phospholipid-coated microcrystals for the sustained release of pharmacologically active compounds and methods of their manufacture and use

## CLAIMS:

7. A method for manufacturing a pharmaceutical composition for the sustained release of a pharmacologically active compound, the composition comprising microcrystals of a pharmacologically active compound contained within a phospholipid layer, the method comprising:

forming a suspension comprising microcrystals of the pharmacologically active compound suspended in a lipid composition; and

passing the suspension through a homogenizer at high pressure to coat the microcrystals with the lipid composition to produce a composition of microcrystals of a pharmacologically active compound contained within a phospholipid layer, wherein

at least about 50 percent of the microcrystals are from about 0.5  $\mu\text{m}$  to about 3  $\mu\text{m}$  in diameter;

at least about ten percent of the microcrystals are from about 3  $\mu\text{m}$  to about 10  $\mu\text{m}$  in diameter; and

the composition contains microcrystals which are greater than about 10  $\mu\text{m}$  in diameter.

8. The method of claim 7 wherein at least about 1% of the microcrystals are greater than about 10  $\mu\text{m}$  in diameter.

9. A method for manufacturing a pharmaceutical composition for the sustained release of a pharmacologically active compound, the composition comprising microcrystals of a pharmacologically active compound contained within a phospholipid layer, the method comprising:

forming a lipid composition; and

contacting the lipid composition with the microcrystals to coat the microcrystals with the lipid composition to produce a composition of microcrystals coated with a phospholipid layer wherein

at least about 50 percent of the microcrystals are from about 0.5  $\mu\text{m}$  to about 3  $\mu\text{m}$  in diameter;

at least about ten percent of the microcrystals are from about 3 .mu.m to about 10 .mu.m in diameter; and the composition contains microcrystals which are larger than about 10 .mu.m in diameter.

10. The method of claim 9 wherein at least about 1% of the microcrystals are greater than about 10 .mu.m in diameter.

11. The method of claim 7 or 10, wherein at least about twenty five percent of the microcrystals are greater than about 3 .mu.m in diameter.

12. The method of claim 7 wherein the composition of lipid and microcrystals is passed through the homogenizer at least two times.

13. The method of claim 7 or 10, wherein the pharmacologically active compound is an antibiotic.

14. The method of claim 13, wherein the antibiotic is oxytetracycline.

15. The method of claim 13 wherein the antibiotic is tilmicosin.

16. The method of claim 13 wherein the antibiotic is a floroquinolone and a cephalosporin covalently combined to form a single molecule.

17. The method of claim 13 wherein the antibiotic is a floroquinolone.

18. The method of claim 17 wherein the floroquinolone is selected from the group consisting of: ofloxacin, sarafloxacin, and ciprofloxacin.

19. The method of claim 13 wherein the antibiotic is a cephalosporin.

20. The method of claim 19 wherein the cephalosporin is cefazolin.

21. The method of claim 19 wherein the cephalosporin is cefuroxime or a derivative of cefuroxime.

22. The method of claim 19 wherein the cephalosporin is cefoperazone.

23. The method of claim 19 wherein the cephalosporin is cefaclor.

24. The method of claim 13 wherein the antibiotic is nitazoxanide.

25. The method of claim 7 or 10, wherein the pharmacologically active compound is an anesthetic.

26. The method of claim 25 wherein the anesthetic is propofol.

27. The method of claims 7 or 10 wherein the pharmacologically active compound is an anti-inflammatory agent.

28. The method of claim 27 wherein the anti-inflammatory agent is flunixin.

29. The method of claims 7 or 10 wherein the pharmacologically active compound is an anti-protozoan agent.

30. The method of claim 29 wherein the anti-protozoan agent is nitazoxanide.

31. The method of claims 7 or 10 further comprising the step of sterilizing the composition of microcrystals.

32. The method of claim 31 wherein the step of sterilizing the composition of microcrystals comprises the use of gamma radiation to sterilize the composition.

33. A method for treating an infection in a mammal comprising the steps of:

administering to the mammal to be treated an effective dose of a composition of microcrystals, the microcrystals comprising an antibiotic and being contained within a phospholipid layer;

wherein at least about 50 percent of the microcrystals are from about 0.5 .mu.m to about 3.0 .mu.m in diameter;

wherein at least about ten percent of the microcrystals are from about 3.0 .mu.m to about 10 .mu.m in diameter; and

the composition contains microcrystals that are larger than about 10 .mu.m in diameter.

34. The method of claim 33 wherein at least about 1% of the microcrystals are larger than about 10 .mu.m in diameter.

35. The method of claim 33 wherein the antibiotic is selected from the group consisting of: oxytetracycline, tilmicosin, cephalone, a floroquinolone, a cephalosporin, or nitazoxanide.

36. The method of claim 33 wherein the composition is administered to the mammal to be treated by parenteral administration.

37. The method of claim 33 wherein the composition is administered to the mammal to be treated by subcutaneous administration.

38. The method of claims 33-35 wherein the mammal is a bovine.

39. The method of claims 33-35 wherein the mammal is an equine.

40. The method of claims 33-35 wherein the mammal is selected from the group consisting of: porcines, canines, and felines.

41. The method of claims 33-35 wherein the infection is caused by a protozoan.

42. A method for treating respiratory disease in a mammal comprising the steps of:

administering to the mammal to be treated an effective dose of a composition of microcrystals, the microcrystals comprising an antibiotic contained within a phospholipid layer; wherein

at least about 50 percent of the microcrystals are from about 0.5 .mu.m to about 3.0 .mu.m in diameter;

at least about ten percent of the microcrystals are from about 3.0 .mu.m to about 10 .mu.m in diameter; and

the composition contains microcrystals that are larger than about 10 .mu.m in diameter.

43. The method of claim 42 wherein at least about 1% of the microcrystals are larger than about 10 .mu.m in diameter.

44. The method of claim 42 wherein the antibiotic is selected from the group consisting of: oxytetracycline, tilmicosin, cephalone, a floroquinolone, a cephalosporin, or nitazoxanide.

45. The method of claim 42 wherein the composition is administered to the mammal to be treated by parenteral administration.

46. The method of claim 42 wherein the composition is administered to the mammal to be treated by subcutaneous administration.

47. The method of claims 42-44 wherein the mammal is a bovine.

48. The method of claims 42-44 wherein the respiratory disease is bovine respiratory disease.

49. The method of claim 42-44 wherein the microcrystals contain oxytetracycline.

50. The method of claims 42-44 wherein the mammal is an equine.

51. The method of claims 42-44 wherein the mammal is selected from the group consisting of: porcines, canines, and felines.

52. A method for treating inflammation in a mammal comprising the steps of:

administering to the mammal to be treated an effective dose of a composition of microcrystals, the microcrystals comprising an anti-inflammatory agent and being contained within a phospholipid layer; wherein

at least about 50 percent of the microcrystals are from about 0.5 .mu.m to about 3.0 .mu.m in diameter;

at least about ten percent of the microcrystals are from about 3.0 .mu.m to about 10 .mu.m in diameter; and

the composition contains microcrystals that are larger than about 10 .mu.m in diameter.

53. The method of claim 52 wherein at least about 1% of the microcrystals are larger than about 10 .mu.m in diameter.

54. The method of claim 52 wherein the composition is administered to the mammal to be treated by parenteral administration.

55. The method of claim 52 wherein the composition is administered to the mammal to be treated by subcutaneous administration.

56. The method of claims 52 or 53 wherein the anti-inflammatory agent is flunixin.

57. A method for treating pain in a mammal comprising the steps of:

administering to the mammal to be treated an effective dose of a composition of microcrystals, the microcrystals comprising an anesthetic and being contained within a phospholipid layer; wherein

at least about 50 percent of the microcrystals are from about 0.5 .mu.m to about 3.0 .mu.m in diameter;

at least about ten percent of the microcrystals are from about 3.0 .mu.m to about 10 .mu.m in diameter; and

the composition contains microcrystals that are greater than about 10 .mu.m in diameter.

58. The method of claim 57 wherein at least about 1% of the microcrystals are greater than about 10 .mu.m in diameter.

59. The method of claim 57 wherein the composition is administered to the mammal to be treated by parenteral administration.

60. The method of claim 57 wherein the composition is administered to the mammal to be treated by subcutaneous administration.

61. The method of claims 57 or 58 wherein the anesthetic is propofol.

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L2: Entry 12 of 17

File: USPT

Oct 27, 1998

DOCUMENT-IDENTIFIER: US 5827543 A

TITLE: Methods and compositions for the prevention and treatment of urogenital disorders

## CLAIMS:

1. A method for treatment of a human or lower animal subject having a urogenital disorder caused or mediated by one or more parasitic protozoa comprising administering to the subject from about 50 milligrams to about 10,000 milligrams of bismuth, per day for from about 1 to 56 days; and from about 100 milligrams to about 10,000 milligrams of each of one or more antimicrobials, per day, for from about 1 to about 28 days.
2. The method of claim 1 wherein the bismuth is administered intravaginally in the form of a suppository at a level of from about 50 milligrams to about 5000 milligrams, per day.
3. The method of claim 2 wherein the bismuth is selected from the group consisting of bismuth aluminate, bismuth subcarbonate, bismuth subcitrate, bismuth citrate, tripotassium dicitrate bismuthate, bismuth subgalate, bismuth subsalicylate, bismuth tartrate, and mixtures thereof.
4. The method of claim 1 wherein each of the one or more antimicrobials is administered orally at a level of from about 100 milligrams to about 8000 milligrams, per day.
5. The method of claim 4 wherein the one or more antimicrobials are selected from the group consisting of penicillin, tetracycline, metronidazole, doxycycline, tinidazole, amoxycillin, ampicillin, nitrofurantoin, and atovaquone.
6. The method of claim 1 wherein the bismuth is administered intravaginally in the form of a douche for from about 2 to 28 days and the one or more antimicrobials are administered in the form of a tablet for from about 1 to about 21 days.
7. The method of claim 1 wherein the parasitic protozoa are selected from the group consisting of *Trichomonas vaginalis*, *Encephalitozoon hellem*, and combinations thereof.
8. A method for prevention in a human or lower animal subject in need thereof, of a urogenital disorder caused or mediated by one or more parasitic protozoa comprising administering to the subject from about 50 milligrams to about 10,000 milligrams of bismuth, per day, for from about 1 to about 21 days; and from about 100 milligrams to about 10,000 milligrams of each of one or more antimicrobials, per day, for from about 1 to about 14 days.

9. The method of claim 8 wherein the bismuth is administered intravaginally in the form of a douche at a level of from about 50 milligrams to about 5000 milligrams, per day.

10. The method of claim 9 wherein the bismuth is selected from the group consisting of bismuth aluminate, bismuth subcarbonate, bismuth subcitrate, bismuth citrate, tripotassium dicitrate bismuthate, bismuth subgallate, bismuth subsalicylate, bismuth tartrate, and mixtures thereof.

11. The method of claim 8 wherein each of the one or more antimicrobials is administered orally at a level of from about 100 milligrams to about 8000 milligrams, per day.

12. The method of claim 11 wherein the one or more antimicrobials are selected from the group consisting of penicillin, tetracycline, metronidazole, doxycycline, tinidazole, amoxycillin, ampicillin, nitrofurantoin, and atovaquone.

13. The method of claim 8 wherein the bismuth is administered for from about 1 to about 14 days and the one or more antimicrobials are administered for from about 1 to about 7 to 10 days.

14. The method of claim 8 wherein the parasitic protozoa are selected from the group consisting of Trichomonas vaginalis, Encephalitozoon hellem, and combinations thereof.

15. The method of claim 1 wherein the subject is administered a composition comprising:

- (a) a safe and effective amount of bismuth;
- (b) a safe and effective amount of one or more antimicrobials;
- (c) pharmaceutically-acceptable carriers materials; and

wherein the safe and effective amount of the bismuth and one or more antimicrobials is effective for treating the urogenital disorder caused or mediated by one or more parasitic protozoa.

16. The method of claim 8 wherein the subject is administered a composition comprising:

- a) a safe and effective amount of bismuth;
- (b) a safe and effective amount of one or more antimicrobials;
- (c) pharmaceutically-acceptable carriers materials; and

wherein the safe and effective amount of the bismuth and one or more antimicrobials is effective for preventing the urogenital disorder caused or mediated by one or more parasitic protozoa.

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L2: Entry 13 of 17

File: USPT

Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811088 A

TITLE: Antiinfective compounds and methods of use

## CLAIMS:

1. A method of treating an infection in a human or animal caused by a bacteria comprising the step of:

administering an effective amount of a composition nonionic block copolymer into the human or animal, wherein the copolymer has the following general formula:

$\text{HO}(\text{C.sub.2 H.sub.4 O})_{\text{sub.b}} (\text{C.sub.3 H.sub.6 O})_{\text{sub.a}} (\text{C.sub.2 H.sub.4 O})_{\text{sub.b}} \text{H}$

wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and approximately 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and approximately 50% of the copolymer.

2. The method of claim 1 wherein a is an integer such that the polyoxypropylene portion represented by  $(\text{C.sub.3 H.sub.6 O})$  has a molecular weight of about 2,250 to 6,000 and b is an integer such that the polyoxyethylene portion represented by  $(\text{C.sub.2 H.sub.4 O})$  constitutes between approximately 5% to 30% by weight of the copolymer.

3. The method of claim 1 wherein a is an integer such that the polyoxypropylene portion represented by  $(\text{C.sub.3 H.sub.6 O})$  has a molecular weight of about 2,250 to 4,000 and b is an integer such that the polyoxyethylene portion represented by  $(\text{C.sub.2 H.sub.4 O})$  constitutes between approximately 10% to 20% by weight of the copolymer.

4. The method of claim 1 wherein a is an integer such that the polyoxypropylene portion represented by  $(\text{C.sub.3 H.sub.6 O})$  has a molecular weight of about 1,200 to 5,300 and b is an integer such that the polyoxyethylene portion represented by  $(\text{C.sub.9 H.sub.4 O})$  constitutes between approximately 10% to 50% by weight of the copolymer.

5. The method of claim 1 wherein a is an integer such that the polyoxypropylene portion represented by  $(\text{C.sub.3 H.sub.6 O})$  has a molecular weight of about 1,750 to 4,500 and b is an integer such that the



polyoxyethylene portion represented by (C.sub.2 H.sub.4 O) constitutes between approximately 10% to 50% by weight of the copolymer.

6. The method of claim 1, wherein the administration of the copolymer is by injection, topical, transdermal, inhalation, trans-mucosal, oral ingestion, and a combination of a plurality of modes of administration.

7. The method of claim 1 wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

8. The method of claim 7 wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

14. The composition of claim 9 wherein the therapeutic drug is selected from the group consisting of rifampin, isoniazid, ethambutol, gentamicin, tetracycline, erythromycin, pyrazinamide, streptomycin, clofazimine, rifabutin, fluoroquinolones such as ofloxacin and sparfloxacin, azithromycin, clarithromycin, dapsone, doxycycline, ciprofloxacin, ampicillin, amphotericin B, fluconazole, ketoconazole, fluconazole, pyrimethamine, sulfadiazine, clindamycin, azithromycin, paromycin, diclazaril, clarithromycin, atovaquone, pentamidine, acyclovir, trifluorouridine, AZT, DDI, DDC, and other antiviral nucleoside analogs, foscarnat, ganciclovir, viral protease inhibitors, antisense and other modified oligonucleotides, and ribavirin.

18. A method of treating a human or animal comprising administering to a human or animal infected with a bacteria a therapeutic drug and a nonionic block copolymer, wherein the block copolymer has the following formula:

$\text{HO}(\text{C.sub.2 H.sub.4 O})_{\text{sub.b}} (\text{C.sub.3 H.sub.6 O})_{\text{sub.a}} (\text{C.sub.2 H.sub.4 O})_{\text{sub.b}} \text{H}$

wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and 50% of the copolymer.

19. The method of claim 18 wherein a is an integer such that the polyoxypropylene portion represented by (C.sub.3 H.sub.6 O) has a molecular weight of about 2,250 to 6,000 and b is an integer such that the polyoxyethylene portion represented by (C.sub.2 H.sub.4 O) constitutes between approximately 5% to 30% by weight of the copolymer.

20. The method of claim 18 wherein a is an integer such that the polyoxypropylene portion represented by (C.sub.3 H.sub.6 O) has a molecular weight of about 2,250 to 4,000 and b is an integer such that the polyoxyethylene portion represented by (C.sub.2 H.sub.4 O) constitutes between approximately 10% to 20% by weight of the copolymer.

21. The method of claim 18 wherein a is an integer such that the polyoxypropylene portion represented by (C.sub.3 H.sub.6 O) has a molecular weight of about 1,200 to 5,300 and b is an integer such that the polyoxyethylene portion represented by (C.sub.2 H.sub.4 O) constitutes between approximately 10% to 50% by weight of the copolymer.

22. The method of claim 18 wherein a is an integer such that the polyoxypropylene portion represented by (C.sub.3 H.sub.6 O) has a molecular weight of about 1,750 to 4,500 and b is an integer such that the polyoxyethylene portion represented by (C.sub.2 H.sub.4 O) constitutes between approximately 10% to 50% by weight of the copolymer.

23. The method of claim 18 wherein the administration of the copolymer and the administration of the therapeutic drug are selected from the group consisting of injection, topical, transdermal, inhalation, trans-mucosal, oral ingestion, and a combination of a plurality of modes of administration.

24. The method of claim 18 wherein the nonionic block copolymer is admixed with approximately 0.1% to approximately 5% by weight/volume of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

25. The method of claim 24 wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

26. The method of claim 18 wherein the therapeutic drug is selected from the group consisting of rifampin, isoniazid, ethambutol, gentamicin, tetracycline, erythromycin, pyrazinamide, streptomycin, clofazimine, rifabutin, fluoroquinolones such as ofloxacin and sparfloxacin, azithromycin, clarithromycin, dapsone, doxycycline, ciprofloxacin, ampicillin, amphotericin B, fluconazole, ketoconazole, fluconazole, pyrimethamine, sulfadiazine, clindamycin, azithromycin, paromycin, diclazaril, clarithromycin, atovaquone, pentamidine, acyclovir, trifluorouridine, azidothymidine, dideoxycytidine, dideoxyinosine and other antiviral nucleoside analogs, foscarnat, ganciclovir, viral protease inhibitors, antisense and other modified oligonucleotides, and ribavirin.

27. The method of claim 18 wherein the therapeutic drug comprises a mixture of several antibiotics.

28. The method of claim 18 wherein the therapeutic drug is admixed with the copolymer.

29. A method of treating an infection in a human or animal caused by a fungus comprising the step of:

administering an effective amount of a composition nonionic block copolymer into the human or animal, wherein the copolymer has the following general formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and approximately 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and approximately 50% of the copolymer.

30. The method of claim 29 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

31. The method of claim 29 wherein the molecular weight represented by the polyoxypropylene portion of the

copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

32. The method of claim 29 wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

33. The method of claim 29 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

34. The method of claim 29, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

35. The method of claim 29 wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

36. The method of claim 35 wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

37. The method of 29, wherein the fungus is a Candida species.

38. The method of claim 37, wherein the Candida species is Candida albicans.

39. A method of treating a human or animal comprising administering to a human or animal infected with a fungus a therapeutic drug and a nonionic block copolymer, wherein the block copolymer has the following formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and 50% of the copolymer.

40. The method of claim 39 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

41. The method of claim 39 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

42. The method of claim 39 wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

43. The method of claim 39 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

44. The method of claim 39, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

45. The method of claim 39 wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

46. The method of claim 45 wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

47. The method of claim 39, wherein the bacteria is selected from the group consisting of Mycobacterium tuberculosis, Mycobacterium avium, Mycobacterium leprae, Chlamydia trachomatis, Chlamydia pneumoniae, Chlamydia psittaci, and Listeria monocytogenes.

48. The method of claim 39, wherein the fungus is a Candida species.

49. The method of claim 48, wherein the Candida species is Candida albicans.

50. A method of treating an infection in a human or animal caused by a protozoa comprising the step of:

administering an effective amount of a composition nonionic block copolymer into the human or animal, wherein the copolymer has the following general formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and approximately 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and approximately 50% of the copolymer.

51. The method of claim 50 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

52. The method of claim 50 wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

53. The method of claim 50, wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

54. The method of claim 50, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,750 to 4,500, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

55. The method of claim 50, wherein the administration of the copolymer is by injection, transdermal, inhalation, trans-mucosal, topical, oral ingestion, and a combination of a plurality of modes of administration.

56. The method of claim 50, wherein the composition further comprises approximately 0.1% to approximately 5% by weight of a surfactant, and approximately 0.5% to approximately 5% by volume of an low molecular weight alcohol.

57. The method of claim 56, wherein the surfactant is polyoxyethylene sorbitan monooleate and the alcohol is ethanol.

58. The method of claim 50, wherein the protozoa is a Toxoplasma species.

59. A method of treating a human or animal comprising administering to a human or animal infected with a protozoa a therapeutic drug and a nonionic block copolymer, wherein the block copolymer has the following formula:



wherein:

i. the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 1,200 and 15,000; and

ii. the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 1% and 50% of the copolymer.

60. The method of claim 59, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 6000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 5% and approximately 30% of the copolymer.

61. The method of claim 59, wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 2250 and approximately 4000, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 20% of the copolymer.

62. The method of claim 59, wherein the molecular weight represented by the polypropylene portion of the copolymer is between approximately 1,200 and 5,300, and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between approximately 10% and 50% of the copolymer.

63. The method of claim 59, wherein the molecular weight represented by the polyoxypropylene portion of the

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Reconnected in file OS 17oct03 07:05:32

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2003/Oct W2  
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\*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.  
File 5:BIOSIS Previews(R) 1969-2003/Oct W2  
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\*File 5: BIOSIS Previews to reload October 2003 with major enhancements. See HELP NEWS005 for further information.  
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File 135:NewsRx Weekly Reports 1995-2003/Oct W2  
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\*File 135: New newsletters are now added. See Help News135 for the complete list of newsletters.  
File 144:Pascal 1973-2003/Oct W1  
(c) 2003 INIST/CNRS  
File 149:TGG Health&Wellness DB(SM) 1976-2003/Sep W3  
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File 156:ToxFile 1965-2003/Oct W2  
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File 159:Cancerlit 1975-2002/Oct  
(c) format only 2002 Dialog Corporation  
\*File 159: Cancerlit ceases updating with immediate effect. Please see HELP NEWS.  
File 162:Global Health 1983-2003/Sep  
(c) 2003 CAB International  
\*File 162: Effective May 1, name changes from CAB Health to Global Health.  
File 164:Allied & Complementary Medicine 1984-2003/Oct  
(c) 2003 BLHCIS  
File 172:EMBASE Alert 2003/Oct W2  
(c) 2003 Elsevier Science B.V.  
File 266:FEDRIP 2003/Sep  
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File 370:Science 1996-1999/Jul W3  
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(c) 2003 American Chemical Society  
\*File 399: Use is subject to the terms of your user/customer agreement. Alert feature enhanced for multiple files, etc. See HELP ALERT.  
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec  
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File 444:New England Journal of Med. 1985-2003/Oct W3

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S1 0 PROVISION?/TI AND PROTOZ?/TI

S2 38 PUTATIV?/TI AND PROTOZO?/TI

S3 0 PROVISION?/TI AND CLASSIFIC?/TI AND PROTOZ?

S4 122 NEW/TI AND PROTOZ?/TI AND HUMAN?

?t s4/9/4 6 8 9 24 43 49 54 61 85 94 97

4/9/4 (Item 4 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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09304237 21041991 PMID: 11200426

**From protozoa to mammalian cells: a new paradigm in the life cycle of intracellular bacterial pathogens.**

Harb O S; Gao L Y; Abu Kwaik Y

Department of Microbiology and Immunology, UKCMC, University of Kentucky, Lexington 40536-0084, USA.

Environmental microbiology (England) Jun 2000, 2 (3) p251-65, ISSN 1462-2912 Journal Code: 100883692

Contract/Grant No.: 5T32CA09509; CA; NCI; R29AI38410; AI; NIAID

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

It is becoming apparent that several intracellular bacterial pathogens of **humans** can also survive within protozoa. This interaction with protozoa may protect these pathogens from harsh conditions in the extracellular environment and enhance their infectivity in mammals. This relationship has been clearly established in the case of the interaction between *Legionella pneumophila* and its protozoan hosts. In addition, the adaptation of bacterial pathogens to the intracellular life within the primitive eukaryotic protozoa may have provided them with the means to infect the more evolved mammalian cells. This is evident from the existence of several similarities, at both the phenotypic and the molecular levels, between the infection of mammalian and protozoan cells by *L. pneumophila*. Thus, protozoa appear to play a central role in the transition of bacteria from the environment to mammals. In essence, protozoa may be viewed as a 'biological gym', within which intracellular bacterial pathogens train for their encounters with the more evolved mammalian cells. Thus, intracellular bacterial pathogens have benefited from the structural and biochemical conservation of cellular processes in eukaryotes. The interaction of intracellular bacterial pathogens and protozoa highlights this conservation and may constitute a simplified model for the study of these pathogens and the evolution of cellular processes in eukaryotes. Furthermore, in addition to being environmental reservoirs for known intracellular pathogens of **humans** and animals, protozoa may be sources of emerging pathogenic bacteria. It is thus critical to re-examine the relationship between bacteria and protozoa to further our understanding of current **human** bacterial pathogenesis and, possibly, to predict the appearance of emerging pathogens. (119 Refs.)

Tags: Animal; **Human** ; Support, U.S. Gov't, P.H.S

Descriptors: \*Bacteria--growth and development--GD; \*Mammals --microbiology--MI; \*Protozoa--microbiology--MI; Amoeba--microbiology--MI; Bacteria--genetics--GE; *Legionella pneumophila*--genetics--GE; *Legionella pneumophila*--growth and development--GD

Record Date Created: 20010126

Record Date Completed: 20010322

4/9/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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08631795 95320322 PMID: 7597182

**Microsporidiosis: a new protozoan disease in persons infected with human immunodeficiency virus (HIV)]**

Microsporidiosis--nowa choroba pierwotniakowa u osob zakazonych ludzkim wirusem uposledzenia odpornosci (HIV).

Rogowska-Szadkowska D; Kramarz P

Zaklad Medycyny Rodzinnej Akademii Medycznej w Bialymstoku.

Przeglad epidemiologiczny (POLAND) 1994, 48 (4) p449-53, ISSN 0033-2100 Journal Code: 0413725

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: POLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

The list of infections, threatening patients with impaired immunological system, especially infected with HIV, prolongs systematically. Since early eighties many authors pay attention to little known type of protozoan: Microspora. More and more often new microsporidia species are described as a cause of disease, especially in patients with AIDS. We present review of literature data concerning species known up to now as pathogenic for man: Encephalitozoon cuniculi, Encephalitozoon hellem, Nosema connori and Nosema corneum, Pleistophora sp., as well as enteropathogenic for AIDS-patients-Enterocytozoon bienewisi and Septata intestinalis. (29 Refs.)

Tags: Animal; Human

Descriptors: \*HIV Seropositivity--complications--CO; \*HIV Seropositivity --microbiology--MI; \*Microsporidia--isolation and purification--IP; \*Microsporidiosis--immunology--IM

Record Date Created: 19950801

Record Date Completed: 19950801

4/9/8 (Item 8 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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08266488 94332549 PMID: 8055239

**New parasites on the block: emerging intestinal protozoa .**

Topazian M; Bia F J

Department of Medicine, Yale School of Medicine, New Haven, CT 06520-8019.

Gastroenterologist (UNITED STATES) Jun 1994, 2 (2) p147-59, ISSN 1065-2477 Journal Code: 9308839

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

Several trends in clinical medicine have converged recently and placed intestinal protozoan infections in a position of increasing importance to health professionals. These trends include the pandemic of human immunodeficiency virus (HIV) infections that cause the acquired immunodeficiency syndrome (AIDS) and result in associated opportunistic infections. The increasing use of powerful chemotherapeutic and immunosuppressive agents to prevent rejection of transplanted tissues in human allograft recipients has predisposed these patients to intestinal parasitic infections, which often become chronic and debilitating. Large numbers of people engage in business, philanthropic work, and vacation travel on a worldwide basis. The number of susceptible, potential human hosts for parasitic infections will continue to increase in the coming years. We reviewed 4 protozoan infections that have recently attracted the interest of clinicians, either because they are newly discovered or because they are increasingly prevalent. These infections include cryptosporidiosis



and recently described infections due to Cyclospora species. The AIDS pandemic has also been associated with both the discovery and the rapid emergence of human microsporidiosis. Isospora belli has received renewed attention because of chronic infections now observed in HIV-infected hosts. (36 Refs.)

Tags: Female; Human ; Male

Descriptors: \*AIDS-Related Opportunistic Infections--parasitology--PS; \*Intestinal Diseases, Parasitic; \*Protozoan Infections

Record Date Created: 19940912

Record Date Completed: 19940912

4/9/9 (Item 9 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07770510 93226003 PMID: 8469253

**Cyclospora species--a new protozoan pathogen of humans .**

Ortega Y R; Sterling C R; Gilman R H; Cama V A; Diaz F

Department of Veterinary Science, University of Arizona, Tucson 85721.

New England journal of medicine (UNITED STATES) May 6 1993, 328 (18) p1308-12, ISSN 0028-4793 Journal Code: 0255562

Comment in N Engl J Med. 1993 Nov 11;329(20) 1504-5; Comment in PMID 8413470; Comment in N Engl J Med. 1993 Nov 11;329(20):1505; Comment in PMID 8413471

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

BACKGROUND. Organisms referred to as "cyanobacterium-like bodies" have now been identified worldwide in the feces of both immunocompetent and immunocompromised patients with diarrhea. Organisms with a similar appearance have been isolated from Peruvian patients since 1985. From 1988 to 1991 we studied prospectively two cohorts of infants and young children infected with this organism. We now attempt to identify it. METHODS. Fecal samples were collected weekly from the children and examined with the use of acid-fast staining and staining with a monoclonal antibody specific for cryptosporidium. Stools positive for cyanobacterium-like bodies were preserved in potassium dichromate and exposed to conditions allowing coccidian sporulation and excystation. Both unsporulated and sporulated oocysts were fixed by freeze-substitution techniques and then examined by electron microscopy. RESULTS. Organisms isolated from the feces of Peruvian patients and two patients from the United States were identified as belonging to the coccidian genus cyclospora, after sporulation and excystation of the oocysts according to standard techniques. Complete sporulation occurred within 5 to 13 days in oocysts maintained in potassium dichromate at 25 or 32 degrees C. Complete excystation resulted in the liberation of two sporozoites from the two sporocysts within each oocyst (cryptosporidia have four naked sporozoites within each oocyst). The presence of organelles characteristic of coccidian organisms was confirmed by electron microscopy. CONCLUSIONS. We have identified organisms of the genus cyclospora that are remarkably similar to cryptosporidia in their morphologic features and the diarrheal disease that they produce in humans. The complete life cycle and epidemiology of this new protozoan parasite remain to be described.

Tags: Animal; Female; Human ; Support, Non-U.S. Gov't

Descriptors: \*Coccidiosis--parasitology--PS; \*Diarrhea--parasitology--PS; \*Eucoccidiida--pathogenicity--PY; Aged; Child, Preschool; Eucoccidiida--isolation and purification--IP; Eucoccidiida--ultrastructure--UL; Feces--parasitology--PS; Infant; Middle Age; Spores--ultrastructure--UL

Record Date Created: 19930511

Record Date Completed: 19930511

4/9/24 (Item 4 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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09367511 BIOSIS NO.: 199497375881

A new protozoosis : **Cyclospora infection.**

AUTHOR: Garavelli P L(a); Amendola G(a); Rocchetti A

AUTHOR ADDRESS: (a)Div. di Malatti Infettive, Ospedale Civile di Alesandria  
\*\*Italy

JOURNAL: Giornale di Malattie Infettive e Parassitarie 45 (9):p968-970  
1993

ISSN: 0017-0321

DOCUMENT TYPE: Article

RECORD TYPE: Citation

LANGUAGE: Italian; Non-English

DESCRIPTORS:

MAJOR CONCEPTS: Epidemiology (Population Studies); Gastroenterology (Human Medicine, Medical Sciences); Parasitology; Pathology; Physiology ; Public Health (Allied Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Sporozoa--Invertebrata, Protozoa, Animalia

ORGANISMS: **human** (Hominidae); *Cryptosporidium muris* (Sporozoa); *Cyclospora* (Sporozoa

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; invertebrates; mammals; microorganisms; primates; protozoans; vertebrates

MISCELLANEOUS TERMS: DIARRHEA; ENTERITIS; EPIDEMIOLOGY; MICROBIOLOGY

CONCEPT CODES:

12508 Pathology, General and Miscellaneous-Inflammation and Inflammatory Disease

14006 Digestive System-Pathology

37052 Public Health: Epidemiology-Communicable Diseases

37400 Public Health: Microbiology

60504 Parasitology-Medical

64002 Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Protozoa

BIOSYSTEMATIC CODES:

35400 Sporozoa

86215 Hominidae

4/9/43 (Item 3 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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05891828 Genuine Article#: XE772 Number of References: 25

Title: **Eimeria** (Protozoa : **Eimeriidae**) from North American sciurids, **Glaucomys sabrinus** and **Tamias townsendii**: With a description of a new species

Author(s): Fuller CA (REPRINT) ; Duszynski DW

Corporate Source: UNIV VIRGIN ISL,DIV SCI & MATH/ST THOMAS//VI/00802

(REPRINT); OREGON STATE UNIV,DEPT ZOOL/CORVALLIS//OR/97331

Journal: JOURNAL OF PARASITOLOGY, 1997, V83, N3 (JUN), P467-470

ISSN: 0022-3395 Publication date: 19970600

Publisher: AMER SOC PARASITOLOGISTS, 810 EAST 10TH STREET, LAWRENCE, KS 66044

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Subfile: CC LIFE--Current Contents, Life Sciences; CC AGRI--Current Contents, Agriculture, Biology & Environmental Sciences

Journal Subject Category: PARASITOLOGY

Abstract: From 1990 to 1991, 11 northern flying squirrels, *Glaucomys sabrinus*, and 30 Townsend's chipmunks, *Tamias townsendii*, were live-trapped, marked, and released in MacDonald Forest, Benton Co., Oregon and their feces at each capture examined for the presence of coccidian parasites. Two eimerians were found in *G. sabrinus*: *Eimeria dorneyi* and a second species we describe here as new. One species, *Eimeria vilasi*, was identified from *T. townsendii*. Sporulated oocysts of the new eimerian are strongly ellipsoidal, pointed at 1 end, and are 47.2 x 25.0 (41-52 x 22-31)  $\mu$  m with ovoidal sporocysts, 19.0 x 10.5 (17-21 x 9-11)  $\mu$  m. A micropyle and oocyst residuum are absent, but, occasionally, a polar granule is present in the oocyst. In the sporocysts, Stieda and substieda bodies are present, as is a

membrane-bound residuum. Sporulated oocysts of *E. dorneyi* are uniformly ellipsoidal, 23.0 x 14.7 (17-26 x 13-16)  $\mu$ m with elongate ellipsoidal sporocysts, 11.6 x 5.7 (9-13 x 5-7)  $\mu$ m. A micropyle and oocyst residuum are absent, but 1 polar granule is present. A Stieda body is present, but sub- and parastieda bodies are absent. The sporocyst residuum is composed of granules in a compact mass. Here we provide phototype (hapantotype) specimens archived in a nationally accredited museum and a line drawing (cartoon) to supplement the one provided by Soon and Dorney because their drawing did not show the sporocyst residuum given in the written description.

Identifiers--Keyword Plus(R): WYOMING GROUND-SQUIRREL;  
SPERMOPHILUS-ELEGANS; APICOMPLEXA

Research Fronts: 95-0395 001 (ADULT FEMALE MICE; EXPRESSION OF  
ESTROGEN-RECEPTOR MESSENGER-RNA; CD3(+)CD25(+) LYMPHOCYTE  
SUBPOPULATION; HUMAN TONSILLAR CELLS; IMMUNE FUNCTION)

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4/9/49 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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06905747 EMBASE No: 1997190138

New protozoan pathogens associated with traveller's diarrhea

LES 'NOUVEAUX' PROTOZOAIRES INTESTINAUX DU VOYAGEUR

Dannaoui E.; Rabodonirina M.; Peyron F.

E. Dannaoui, Laboratoire de Parasitologie, Universite Claude Bernard, 8

Avenue Rockefeller, 69373 Lyon France

Medecine et Hygiene ( MED. HYG. ) (Switzerland) 1997, 55/2165

(1096-1102)

CODEN: MEHGA ISSN: 0025-6749

DOCUMENT TYPE: Journal; Short Survey

LANGUAGE: FRENCH SUMMARY LANGUAGE: FRENCH; ENGLISH

NUMBER OF REFERENCES: 17

Three protozoans have recently been identified as causing traveler's diarrhea: *Cryptosporidium parvum*, *Cyclospora cayentanesis*, *Microsporidia* group: (*Encephalitozoon intestinalis* and *Enterocytozoon bienersi*). The pathogenesis of these parasites remains to be elucidated. Nevertheless for investigating chronic diarrhea, it is logical to perform Ziehl Neelsen and Van Gool staining for the diagnosis of *Cryptosporidium* and *Microsporidia*. Direct examination with confirmation of autofluorescence under ultraviolet light, detects *Cyclospora*.

BRAND NAME/MANUFACTURER NAME: bactrim; humagel; humatin; zentel

DRUG DESCRIPTORS:

\*albendazole--drug therapy--dt; \*cotrimoxazole--drug therapy--dt; \*  
paromomycin--drug therapy--dt

MEDICAL DESCRIPTORS:

\*protozoal infection; \*traveller diarrhea--diagnosis--di; \*traveller  
diarrhea--etiology--et; \*traveller diarrhea--drug therapy--dt; \*traveller  
diarrhea--epidemiology--ep  
clinical feature; cryptosporidium parvum; cyclospora; **human** ;  
microbiological examination; microspora; oral drug administration; short  
survey

CAS REGISTRY NO.: 54965-21-8 (albendazole); 8064-90-2 (cotrimoxazole);  
11035-13-5, 1263-89-4, 1390-73-4, 51795-47-2, 54597-56-7, 7542-37-2,  
84420-34-8 (paromomycin)

SECTION HEADINGS:

004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
048 Gastroenterology  
037 Drug Literature Index

4/9/54 (Item 6 from file: 73)

DIALOG(R) File 73:EMBASE

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04289799 EMBASE No: 1990172355

**Royal Society of Tropical medicine and Hygiene meeting at Manson House,  
London, 16 March 1989. New intestinal protozoa - coccidia and  
microsporidia. Enterocytozoon bienewisi (Microspora): Prevalence and  
pathogenicity in AIDS patients**

Canning E.U.; Hollister W.S.

Department of Pure and Applied Biology, Imperial College of Science,  
Technology and Medicine, Prince Consort Road, London SW7 2AZ United  
Kingdom

Transactions of the Royal Society of Tropical Medicine and Hygiene (  
TRANS. R. SOC. TROP. MED. HYG. ) (United Kingdom) 1990, 84/2 (181-186)

CODEN: TRSTA ISSN: 0035-9203

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Microsporidia are unicellular organisms, which lack mitochondria. They  
have prokaryotic-like ribosomes and characteristic spores containing an  
extrusible polar tube which serves as a passage for inoculation of the  
infectious agent (sporoplasm) into host cells. Clinically apparent  
infections in man appear to be limited to immunoprivileged sites or  
immunocompromised patients. One species, *Encephalitozoon cuniculi*, has been  
reported several times in patients with neurological disorders and once  
causing a fatal hepatitis in an AIDS patient. The most recently discovered  
species, *Enterocytozoon bienewisi*, is known only from the small intestinal  
enterocytes of patients with the acquired immunodeficiency syndrome, and is  
easily differentiated from other microsporidia by the precocious  
development of spore organelles in the sporont and by the poor development  
of the endospore layer of the spore wall. Although only about 40 cases have  
been reported, circumstantial evidence suggests that *E. bienewisi* may be the  
cause of a severe watery diarrhoea, which responds only temporarily to  
treatment with metronidazole.

DRUG DESCRIPTORS:

\*metronidazole--drug therapy--dt

MEDICAL DESCRIPTORS:

\*acquired immune deficiency syndrome--complication--co; \*diarrhea--etiology  
--et; \*intestine cell; \*microsporium; \*taxonomy  
classification; histology; ultrastructure; **human** ; protozoon; conference  
paper; priority journal; fungus; drug therapy

CAS REGISTRY NO.: 39322-38-8, 443-48-1 (metronidazole)

SECTION HEADINGS:

004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
047 Virology  
037 Drug Literature Index

4/9/61 (Item 4 from file: 94)  
DIALOG(R)File 94:JICST-EPlus  
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03170958 JICST ACCESSION NUMBER: 97A0411380 FILE SEGMENT: JICST-E  
**Test of new intestinal parasitic protozoa .**  
IZEKI MOTOHIRO (1)  
(1) Osaka City Univ., Med. Sch.  
Kensa to Gijutsu(Modern Medical Laboratory), 1997, VOL.25,NO.4,  
PAGE.335-341, FIG.4, TBL.5, REF.7  
JOURNAL NUMBER: Z0084BAY ISSN NO: 0301-2611  
UNIVERSAL DECIMAL CLASSIFICATION: 616-078  
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan  
DOCUMENT TYPE: Journal  
ARTICLE TYPE: Commentary  
MEDIA TYPE: Printed Publication  
DESCRIPTORS: Coccidia; microorganism test; intestinal disease; protozoan  
infection; optical microscopy; **human** (primates); zygote; biological  
sample staining  
BROADER DESCRIPTORS: Sporozoa; Protozoa; microorganism; inspection;  
gastrointestinal disease; digestive system disease; disease; parasitic  
disease; infectious disease; microscopy; observation and view;  
reproductive cell; cell(cytology); dyeing  
CLASSIFICATION CODE(S): GC02030H

4/9/85 (Item 1 from file: 149)  
DIALOG(R)File 149:TGG Health&Wellness DB(SM)  
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01427585 SUPPLIER NUMBER: 14438608 (THIS IS THE FULL TEXT)  
**Cyclospora species - a new protozoan pathogen of humans . (N Engl J**  
**Med 1993;328:1308-1312) (Abstract)**  
Ortega, Ynes R.  
JAMA, The Journal of the American Medical Association, v270, n12, p1419(1)  
Sept 22,  
1993  
DOCUMENT TYPE: Abstract PUBLICATION FORMAT: Magazine/Journal ISSN:  
0098-7484 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE:  
Professional  
WORD COUNT: 274 LINE COUNT: 00024

TEXT:

Background. Organisms referred to as "cyanobacterium-like bodies" have now been identified worldwide in the feces of both immunocompetent and immunocompromised patients with diarrhea. Organisms with a similar appearance have been isolated from Peruvian patients since 1985. From 1988 to 1991 we studied prospectively two cohorts of infants and young children infected with this organism. We now attempt to identify it.

Methods. Fecal samples were collected weekly from the children and examined with the use of acid-fast staining and staining with a monoclonal antibody specific for cryptosporidium. Stools positive for cyanobacterium-like bodies were preserved in potassium dichromate and exposed to conditions allowing coccidian sporulation and excystation. Both unsporulated and sporulated oocysts were fixed by freeze-substitution techniques and then examined by electron microscopy.

Results. Organisms isolated from the feces of Peruvian patients and two patients from the United States were identified as belonging to the coccidian genus cyclospora, after sporulation and excystation of the oocysts according to standard techniques. Complete sporulation occurred within 5 to 13 days in oocysts maintained in potassium dichromate at 25 or 32[degrees]C. Complete excystation resulted in the liberation of two sporozoites from the two sporocysts within each oocyst (cryptosporidia have four naked sporozoites within each oocyst). The presence of organelles characteristic of coccidian organisms was confirmed by electron microscopy.

Conclusions. We have identified organisms of the genus cyclospora that are remarkably similar to cryptosporidia in their morphologic features and the diarrheal disease that they produce in **humans** . The complete life

cycle and epidemiology of this new protozoan parasite remain to be described.

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DESCRIPTORS: Protozoa, Pathogenic--Identification; Diarrhea--Causes of  
FILE SEGMENT: MI File 47

4/9/94 (Item 3 from file: 162)  
DIALOG(R) File 162:Global Health  
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00661326 CAB Accession Number: 990800696

**Introduction to a new protozoa Enterocytozoon bienersi, a chronic diarrhoea pathogen.**

Qiu YuRong; Zong YueQi  
Chinese Journal of Parasitic Disease Control vol. 11 (2): p.149-150  
Publication Year: 1998  
ISSN: 1001-6627  
Language: Chinese  
Document Type: Journal article  
14 ref.

DESCRIPTORS: diarrhoea; human diseases; pathology; parasites  
ORGANISM DESCRIPTORS: man; Enterocytozoon bienersi; protozoa  
BROADER TERMS: Homo; Hominidae; Primates; mammals; vertebrates; Chordata;  
animals; Enterocytozoon; Enterocytozoonidae; Microspora; Protozoa;  
invertebrates  
CABICODES: Parasites, Vectors, Pathogens & Biogenic Diseases of Humans  
(VV200)

4/9/97 (Item 6 from file: 162)  
DIALOG(R) File 162:Global Health  
(c) 2003 CAB International. All rts. reserv.

00634969 CAB Accession Number: 980803679

**Cyclospora cayentanensis: A new protozoan pathogen causing diarrhoea.**

Wanachiwanawin, D.  
Siriraj Hospital Gazette vol. 49 (4): p.377-381  
Publication Year: 1997  
ISSN: 0125-152X  
Language: Thai  
Document Type: Journal article  
24 ref.

DESCRIPTORS: human diseases; diarrhoea  
ORGANISM DESCRIPTORS: Cyclospora cayentanensis; man  
BROADER TERMS: Cyclospora; Eimeriidae; Eucoccidiorida; Apicomplexa;  
Protozoa; invertebrates; animals; Homo; Hominidae; Primates; mammals;  
vertebrates; Chordata  
CABICODES: Parasites, Vectors, Pathogens & Biogenic Diseases of Humans  
(VV200)

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$0.05      Estimated cost File135
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$0.03      Estimated cost File144
$0.04      $0.04      0.010 DialUnits File149
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$0.03      Estimated cost File159
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$0.06      Estimated cost File467
$0.22      OneSearch, 26 files, 0.337 DialUnits FileOS
$0.22      TELNET
$24.08     Estimated cost this search
$24.08     Estimated total session cost 0.337 DialUnits

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### Status: Signed Off. (1 minutes)

04289799 EMBASE No: 1990172355

Royal Society of Tropical medicine and Hygiene meeting at Manson House, London, 16 March 1989. New intestinal protozoa - coccidia and microsporidia. Enterocytozoon bienewi (Microspora): Prevalence and pathogenicity in AIDS patients

Canning E.U.; Hollister W.S.

Department of Pure and Applied Biology, Imperial College of Science, Technology and Medicine, Prince Consort Road, London SW7 2AZ United Kingdom

Transactions of the Royal Society of Tropical Medicine and Hygiene ( TRANS. R. SOC. TROP. MED. HYG. ) (United Kingdom) 1990, 84/2 (181-186)

CODEN: TRSTA ISSN: 0035-9203

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Microsporidia are unicellular organisms, which lack mitochondria. They have prokaryotic-like ribosomes and characteristic spores containing an extrusible polar tube which serves as a passage for inoculation of the infectious agent (sporoplasm) into host cells. Clinically apparent infections in man appear to be limited to immunoprivileged sites or immunocompromised patients. One species, Encephalitozoon cuniculi, has been reported several times in patients with neurological disorders and once causing a fatal hepatitis in an AIDS patient. The most recently discovered species, Enterocytozoon bienewi, is known only from the small intestinal enterocytes of patients with the acquired immunodeficiency syndrome, and is easily differentiated from other microsporidia by the precocious development of spore organelles in the sporont and by the poor development of the endospore layer of the spore wall. Although only about 40 cases have been reported, circumstantial evidence suggests that E. bienewi may be the cause of a severe watery diarrhoea, which responds only temporarily to treatment with metronidazole.



YSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2003/Oct W2

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\*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

File 5:Biosis Previews(R) 1969-2003/Oct W2

(c) 2003 BIOSIS

\*File 5: BIOSIS Previews to reload October 2003 with major enhancements. See HELP NEWS005 for further information.

File 73:EMBASE 1974-2003/Oct W2

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File 162:Global Health 1983-2003/Sep

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\*File 162: Effective May 1, name changes from CAB Health to Global Health.

File 50:CAB Abstracts 1972-2003/Sep

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\*File 50: Truncating CC codes is recommended for full retrieval. See Help News50 for details.

File 144:Pascal 1973-2003/Oct W1

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File 10:AGRICOLA 70-2003/Oct

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File 94:JICST-EPlus 1985-2003/Oct W2

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File 440:Current Contents Search(R) 1990-2003/Oct 17

(c) 2003 Inst for Sci Info

File 349:PCT FULLTEXT 1979-2002/UB=20031009,UT=20031002

(c) 2003 WIPO/Univentio

Set Items Description

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Cost is in DialUnits

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Set	Items	Description
S1	201	URETHRITIS?/TI AND PROTOZ?
S2	141	RD (unique items)
S3	1	S2 AND PH AND (SIZE OR MICRON? OR EXTRACELLULAR?)
?t s2/9/1-2 5 6 18 24 26 28 93 94		

**WEST**

Generate Collection

L30: Entry 20 of 81

File: USPT

Nov 9, 1999

DOCUMENT-IDENTIFIER: US 5981300 A

TITLE: Test kit for analyzing body fluids and analysis method

Brief Summary Text (41):

In a particularly inexpensive embodiment that is easy to handle by the consumer, the means for determining the pH value of the saliva removed is in the form of test paper for determining the pH value. Thus, a test zone may be provided which changes to different colors when liquids with different pH values are applied. Colored comparison boxes enable the pH value to be quickly and reliably determined. Corresponding test papers are inexpensive because they are mass-produced.

**WEST**☐

Generate Collection

L19: Entry 4 of 101

File: USPT

Apr 15, 2003

DOCUMENT-IDENTIFIER: US 6547803 B2

TITLE: Microfabricated surgical device for interventional procedures

Detailed Description Text (32):

Various microfabricated devices can be integrated into the needle, actuator and catheter for metering flows, capturing samples of biological tissue, and measuring pH. The device 10, for instance, could include electrical sensors for measuring the flow through the microneedle as well as the pH of the pharmaceutical being deployed. The device 10 could also include an intravascular ultrasonic sensor (IVUS) for locating vessel walls, and fiber optics, as is well known in the art, for viewing the target region. For such complete systems, high integrity electrical, mechanical and fluid connections are provided to transfer power, energy, and pharmaceuticals or biological agents with reliability.

**WEST**

Generate Collection

L29: Entry 2 of 26

File: USPT

Feb 12, 2002

DOCUMENT-IDENTIFIER: US 6346106 B1

TITLE: Instrument and method employing snare electrode windable about rotatable spool for minimally invasive electrosurgical resection

Abstract Text (1):

A surgical instrument includes a body, a snare electrode, a spool and an electrical connector. A distal part of the body includes a passageway extending axially therethrough. The snare electrode is adapted to telescope in the passageway. The distal part of the body has an outward surface electrically insulated from the snare electrode. A second portion of the snare electrode is extendable from a second port of the passageway for forming a loop sized to be placed over tissue (e.g., portion(s) of the uterus and/or kidney(s), spleen, pancreas, gallbladder, remnant from the liver, and/or vascular aneurysm) to be removed from a patient. The spool is rotatably supported in a proximal part of the body. A first portion of the snare electrode is windable about the spool. A rotation of the spool in a winding direction causes retraction of the first portion of the snare electrode from a first port of the passageway, thereby closing the loop to engage the tissue. The electrical connector is for allowing the snare electrode to be coupled to an electrical source. An electrical current is passed from the electrical source to the loop to cauterize the tissue.

Detailed Description Text (28):

For instance, the attachment 134 might include a spreader or shield 134 which may be used during the surgery to move tissue surrounding the targeted tissue 120 to be resected, and to create more room to operate. Further, a receptacle slot of the "bipolar" head 132B and a stem of the attachment 134 might have mating screwthreads. For example, the shield 134 might safeguard patient 126 while companion electrode 106 is passed (e.g., in the cervical canal of a female for surgery to resect a uterus) to a desired interior location of the patient, to complete the electrical circuit. The shield 134 might have any desired dimension(s). An exemplary shield 134 might be disk-shaped with a transverse dimension (e.g., a diameter) which is sufficient to allow the shield 134 to separate or move tissue(s) away from an organ to be resected. For example, in the case of resection of the uterus, the shield 134 may separate surrounding tissues from the uterus so that the instrument 102 and/or the companion electrode 106 may be maneuvered into the proper position. The attachment 134 may comprise a cap 111.

Detailed Description Text (33):

The instrument 102 and/or companion electrode 106, if operated in a "bipolar" mode, might be passed through the incision. Such a technique may be used in the abdomen to remove a relatively large tumor (e.g., myofibroma or leiomyoma) 120, or within the uterus of a female. For example, the companion electrode might be passed in the cervical canal of the female. In particular, head 132B and insulated handle 107 may be inserted into and partially through the vagina.

Detailed Description Text (43):

Surgical instrumentation 100 might be utilized, for example, in performance of hysterectomies, laparoscopic

surgeries, and/or standard or classical operations. In particular, the surgical instrumentation 100 might serve to resect portions (e.g., some or all) of the uterus and/or kidney(s), spleen, pancreas, gallbladder, remnant from the liver, vascular aneurysm or tonsil. For instance, the surgical instrumentation can advantageously decrease invasiveness of removing a relatively large tumor, including malignant tumors, such as might be present on the uterus. When the surgical instrumentation is used to perform hysterectomies, the upper portion of the uterus may be cut to perform a partial resection and/or another cut may be made below the cervix at the cervical fornix for a total resection of the uterus.

Detailed Description Text (44):

In one aspect of the present invention, companion electrode 106 may be operated without attachment 134, and neck 109 (FIG. 1) may be selected to comprise a small conductive (e.g., metal) surface area. The neck may be exposed in order to coagulate certain pathological tissue in the cervical canal, in accordance with the principles of the present invention. Then, the attachment 134 may be connected to the companion electrode 106, such as with mating screw threads, and pressed against the cut cervical surface to provide temporary hemostasis. Preferably, part(s) of the attachment 134 which contact patient 126 are covered or formed with plastic insulator, to avoid potential electric shock. In one example, section(s) of the attachment which do not contact the patient may be formed from metal.

Detailed Description Text (45):

In another aspect, referring to FIG. 1, first companion electrode 106 with attachment 134 can be operated in a "monopolar" mode with a second companion return electrode 106 having exterior head 132A, which may comprise a large adhesive return electrode pad. In particular, the first companion electrode may serve as the active electrode, which may be pressed against the cut stump of the uterine cervix. Furthermore, one may ablate additional tissue, deeper in the cervical canal, by employing the first companion electrode without the attachment connected thereto and with neck 109 exposed, as described above.

**CLAIMS:**

8. The instrument of claim 3, further comprising a casing for said driver, wherein said casing includes at least one of an outward surface electrically insulated from said snare electrode and a handle.

28. The instrument of claim 23, further comprising a casing for said driver, wherein said casing includes at least one of an outward surface electrically insulated from said snare electrode and a handle.

WEST



Generate Collection

Print

L29: Entry 3 of 26

File: USPT

Feb 12, 2002

DOCUMENT-IDENTIFIER: US 6346105 B1

TITLE: Device for treating tissue and methods thereof

Abstract Text (1):

A medical device for treating the hemorrhoid, or reducing the dilatation of cellular tissues comprising ligating a hemorrhoid tissue and heating the hemorrhoid tissue. In one embodiment, an elongate tubular shaft comprises at least one coil loop electrode arrangement disposed at the distal end portion of the shaft, a RF energy generating source, and a method for deploying a dilated ligature element to effect the pressure therapy for the hemorrhoid tissues.

Brief Summary Text (7):

Of particular interest to the present invention are RF therapeutic protocols, which have been proven to be highly effective when used by electrophysiologists for the treatment of tachycardia; by neurosurgeons for the treatment of Parkinson's disease; and by neurosurgeons and anesthesiologists for other RF procedures such as Gasserian ganglionectomy for trigeminal neuralgia and percutaneous cervical cordotomy for intractable pains. Radiofrequency treatment, which exposes a patient to minimal side effects and risks, is generally performed after first locating the tissue sites for treatment. Radiofrequency or other energy, when coupled with a temperature control mechanism, can be supplied precisely to the device-to-tissues contact site to obtain the desired temperature for treating a tissue.

## CLAIMS:

1. A medical device system comprising:

a delivery tubular shaft having a distal section, a distal end, a proximal end, and at least one lumen extending therebetween;

a handle attached to the proximal end of the delivery tubular shaft, wherein the handle has a cavity;

an inner elongate tubular shaft located within the at least one lumen of the delivery tubular shaft, the inner elongate tubular shaft, on which thereof an electrode means for treating tissue is mounted on a distal end portion, an electrical conductor passing through the inner elongate tubular shaft and connected to the electrode means, and mounted on a proximal end portion of the delivery tubular shaft to the handle of the device, wherein the electrode means comprises at least one compressible coil loop arrangement having a distal end portion to contact a target tissue, the compressible coil loop arrangement having the capability of applying appropriate pressure to encircle and press the target tissue;

an elastic dilated ligature element circumferentially and externally positioned at about the distal section of the delivery tubular shaft, wherein said dilated ligature element is pushed off the distal section of the delivery tubular shaft at a deployed state; and

a RF energy generating means, wherein the RF energy is provided to the electrode means through the electrical conductor.

9. A method of treating a hemorrhoid of a patient, the method comprising:

(a) placing a medical device system against the hemorrhoid of the patient, wherein the medical device comprises a delivery tubular shaft having a distal section, a distal end, a proximal end, and at least one lumen extending therebetween; a handle attached to the proximal end of the delivery tubular shaft, wherein the handle has a cavity; an inner elongate tubular shaft located within the at least one lumen of the delivery tubular shaft, the inner elongate tubular shaft, on which thereof an electrode means for treating tissue is mounted on a distal end portion, an electrical conductor passing through the inner elongate tubular-shaft and connected to the electrode means, and mounted on a proximal end portion of the delivery tubular shaft to the handle of the device, wherein the electrode means comprises at least one compressible coil loop arrangement having a distal end portion to contact a target tissue, the compressible coil loop arrangement having the capability of applying appropriate pressure to encircle and press the target tissue; an elastic dilated ligature element circumferentially and externally positioned at about the distal section of the delivery tubular shaft, wherein said dilated ligature element is pushed off the distal section of the delivery tubular shaft at a deployed state; and a RF energy generating means, wherein the RF energy is provided to the electrode means through the electrical conductor;

(b) applying an appropriate pressure on the at least one compressible coil loop arrangement to encircle and press the target tissue;

(c) deploy the dilated ligature element to be off the distal section of the delivery tubular shaft to ligate the hemorrhoid; and

(d) applying RF energy to the tissues encircled under the exposed coil loop region to effect treatment of the hemorrhoid.

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**Improved diagnosis of Trichomonas vaginalis infection by PCR using vaginal swabs and urine specimens compared to diagnosis by wet mount microscopy, culture, and fluorescent staining.**

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Four vaginal cotton swab specimens were obtained from each of 804 women visiting the outpatient sexually transmitted disease clinic of the Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands, for validation of various forms of *Trichomonas vaginalis* diagnostic procedures. One swab specimen was immediately examined by wet mount microscopy, a second swab was placed in Kupferberg's Trichosel medium for cultivation, and two swabs were placed in phosphate-buffered saline (PBS), pH 7.2. The resulting PBS suspension was used for direct staining with acridine orange and fluorescence microscopy, inoculation of modified Diamond's culture medium, and a PCR specific for *T. vaginalis*. A total of 70 samples positive in one or more of the tests were identified: 31 (3.8%) infections were detected by wet mount microscopy, and 36 (4.4%) were identified by acridine orange staining, as opposed to 40 (4.9%) and 46 (5.7%) positives in modified Diamond's and Trichosel media, respectively. PCR was positive for 61 (7.5%) samples. Secondly, from each of 200 women were obtained a urine sample and a vaginal cotton swab specimen, and 200 urine samples were obtained from men. For the women, 15 (7.4%) of the samples showed a positive result for either the wet mount (n = 1), Trichosel culture (n = 6), PCR on the vaginal swab sample (n = 10), or PCR on the urine specimen (n = 11). Four men (2%) were diagnosed with a *T. vaginalis* infection. Thus, PCR appears to be the method of choice for the detection of genital infections with *T. vaginalis*.